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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,610	09/16/2003	Charles Wilson	23239-538 (ARC-38)	5499

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,610	WILSON ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *127-137* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *127-137* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the response filed on 26 March 2009. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Claims 1-126 have been cancelled. Claims 127-137 have been added. Claims 127-137 are pending and are currently under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 46-57, 60-64, 66, 69-111 and 113-126 under 35 U.S.C. §103(a) as being obvious over Griffin et al. (U.S. Patent No. 5,756,291, hereinafter "Griffin") is withdrawn in view of Applicants' cancellation of the claims.

Applicant's arguments with respect to claims 46-57, 60-64, 66, 69-111 and 113-126 have been considered but are moot in view of the new grounds of rejection.

NEW REJECTION

Claims 127-130, 133, 136 and 137 are rejected under 35 U.S.C. §103(a) as being unpatentable over Sullenger *et al.* (US 2003/0083294 A1, effectively filed 25 May 2001).

The instant claims are drawn to a method for identifying an aptamer regulator comprising:

a) contacting a mixture of nucleic acids with a target and a target partner under conditions that disfavor efficient binding between the target and the target partner;

b) partitioning nucleic acids bound to a target-target partner complex from unbound nucleic acids; and

c) retaining the nucleic acids bound to the target-target partner complex, thereby identifying an aptamer that binds to a target wherein binding of the aptamer to the target increases the binding affinity of the target for the target partner relative to the affinity of the target for the target partner when the target is not bound by the aptamer.

Sullenger *et al*. discloses a method to identify modulators of nucleic acid ligands (paragraphs [0024]) so that, upon binding, the three dimensional structure of the nucleic acid ligand is altered so that the affinity of the nucleic acid ligand for its target molecule is enhanced ([0071]). In one embodiment, the modulator itself is an aptamer ([0022]). After a nucleic acid ligand is generated to bind to the desired therapeutic target, a second nucleic acid ligand (meeting the claim limitation of the aptamer regulator) that binds to the first nucleic acid ligand is generated using the SELEX process (meeting the limitations in claimed step b and c) and modulates the interaction between the therapeutic nucleic acid ligand (meeting the claim limitation of target) and its target (meeting the claim limitation of target partner). The modulator can be contacted with the targeted nucleic acid ligand under conditions such that it binds to the nucleic acid

ligand and modifies the interaction between the nucleic acid ligand and its target molecule ([0069]). Modulators can be designed so as to bind any particular nucleic acid ligand with a high degree of specificity and a desired degree of affinity ([0070]). The binding or interaction of the modulator with the nucleic acid ligand is measured by evaluating the effect of the ligand with and without the regulator under appropriate biological conditions in BIACORE assays ([0074] and [0115]), which meets the claim limitation of the step of screening the retained nucleic acids for a desired functional activity. Using the same general selection scheme, the SELEX method can be used to achieve virtually any desired criterion of binding affinity and selectivity ([0004]). The SELEX process starts with a candidate mixture of oligonucleotides containing a region that corresponds to an oligonucleotide modulator of interest and a randomized region of sequences ([0004] and [0115]), which meets the claim limitation of diversified target-specific pool of nucleic acids, and the SELEX method includes steps of contacting the mixture with the target under conditions favorable for binding, partitioning unbound nucleic acids from those nucleic acids that have bound specifically to target molecules, amplifying the nucleic acids dissociated from the nucleic acid-target complexes, then iterating the steps of binding, partitioning, dissociating and amplification through as many cycles as desired ([0004]).

Although Sullenger *et al*. does not *ipsis verbis* disclose the phrase "conditions that disfavor efficient binding between the target and the target partner" in claimed step a, the disclosure of contacting conditions, such that the modulator binds to the nucleic

acid ligand and enhances the interaction between the nucleic acid ligand and its target molecule, implicitly teaches the conditions in the claimed invention.

Although Sullenger *et al*. does not disclose immobilizing the target partner, Sullenger *et al*. suggests immobilizing the target nucleic acid ligand on a solid support ([0158]) so that the binding can be confirmed by appropriate bioassays.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the aptamer modulator SELEX method disclosed by Sullenger *et al*. by immobilizing the target partner instead of the target (nucleic acid ligand) with a reasonable expectation of success because the function to be selected is the binding between a target and its target partner facilitated by an aptamer. Either the target or target partner being immobilized would be detectable in the BIOCORE binding assay. The skilled artisan would have been motivated to do so in order to partition and retain aptamer regulators bound to the target-target partner complex, all of which would be bound to the immobilizing solid support, while unbound aptamers would not. It would also have been obvious to use a nucleic acid ligand as the target in the SELEX method with the specific suggestions per Sullenger *et al*., to select for aptamer modulators that enhance the binding of nucleic acid target to its target partner. In addition, a person having ordinary skill in the art would be familiar with the conditions, such as the concentration of the target molecules and the pH and salt concentration of the solution of the incubation mixture, that favor and disfavor binding, which would vary depending upon the target and target partner. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 131 and 132 are rejected under 35 U.S.C. §103(a) as being unpatentable over Sullenger *et al*. (US 2003/0083294 A1, effectively filed 25 May 2001) in view of Griffin *et al*. (U.S. Patent No. 5,756,291, patented 26 May 1998).

The instant invention further comprises a negative selection that removes nucleic acids that bind to target partner alone.

The disclosure of Sullenger *et al*. is set forth above. Sullenger *et a*l. does not disclose negative selection.

Griffin *et al*. discloses a negative selection step before a positive selection step in a modified SELEX method (column 29, lines 17-27), mixing the original oligonucleotide mixture with the undesired substance to complex away the members of the oligonucleotide mixture which bind to the undesired substance; the unbound oligonucleotides are then recovered and amplified and incubated with the target under conditions wherein those members of the oligonucleotide mixture which bind targets are complexed.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the aptamer modulator SELEX method disclosed by Sullenger *et al*. by adding a round of negative selection prior to the selection for aptamer regulator with a reasonable expectation of success because Griffin *et al*. provides the motivation, teaching, and suggestion, that it is often advantageous in enhancing the specificity of the aptamer obtained to remove members of the starting oligonucleotide mixture which bind to a second undesired substance from which the

target molecule is to be distinguished. This method is particularly useful in obtaining aptamers which bind to targets that reside on cell surfaces since a large number of contaminating materials will surround the desired target (column 28, lines 60-67). When the method is applied in this case, the undesired second substance would be the target or target partner alone and the desired target molecule would be the target and target partner together. The function to be selected is the binding between a target and its target partner facilitated by an aptamer. It would also have been obvious to use a nucleic acid ligand as the target in the SELEX method with the specific suggestions per Sullenger *et al.*, to select for aptamer modulators that enhance the binding of nucleic acid target to its target partner. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 133-135 are rejected under 35 U.S.C. §103(a) as being unpatentable over Sullenger *et al.* (US 2003/0083294 A1, effectively filed 25 May 2001) in view of Gold *et al.* (U.S. Patent No. 5,763,173, patented 9 June 1998, No. A28 in IDS filed 22 May 2006, hereinafter '173).

The instant invention limits the step of removing the retained nucleic acids from the target-target partner complex by eluting the nucleic acids with an agonist competitor to the target.

The disclosure of Sullenger *et al.* is set forth above. Sullenger *et al.* is silent on the exact procedure in the step of dissociating the nucleic acid-target complexes. In other words, Sullenger *et al.* does not specifically disclose the approach of eluting the

nucleic acids with a competitor to the target. However, Sullenger *et al*. discloses that the SELEX process was first described by Gold and Tuerk ([0003]).

Gold patent '173 discloses the specific procedure of eluting bound DNA aptamers with a target competitor, tRNA, to the target polymerase (column 9, lines 15-26).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the aptamer modulator SELEX method disclosed by Sullenger *et al*., by eluting the nucleic acids with an agonist competitor to the target, as taught by the Gold patent '173, with a reasonable expectation of success because Sullenger *et al*. specifically refers to the patents to Gold for details of the SELEX method. It would also have been obvious to one of ordinary skill in the art to substitute the target competitor with excess free target to elute bound nucleic acids since the excess free target is also a competitor to the target that is attached to a solid support. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LOUISE HUMPHREY whose telephone number is (571)272-5543. The examiner can normally be reached on Mon-Thu, 9:00 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Jeffrey S. Parkin/
Primary Examiner, Art Unit 1648

31 March 2009